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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,485	10/17/2001	Brenda F. Baker	RTS-0139	5056

7590 01/26/2004

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EXAMINER

EPPS FORD, JANET L

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 01/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/035,485

Applicant(s)

BAKER ET AL.

Examiner

Janet L. Epps-Ford, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-10 and 12-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-10 and 12-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 103

2. Claims 1-2, and 4-10 and 12-14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Khaw et al. in view of Brinckerhoff et al. and Monia et al.
3. Applicant's arguments filed 11-13-03 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the primary references and the secondary references, when combined, do not teach or suggest the invention of the claims as amended which are targeted to a specific region (i.e. a coding region) within the sequence of SEQ ID NO: 3. Moreover, Applicants argue that it is only with the specification in hand that one of skill would be able to know that the compounds of the claimed invention could be used successfully to inhibit expression of SEQ ID NO: 3.

Contrary to Applicant's assertions, the prior art cited clearly provide motivation for designing antisense oligonucleotides targeting a nucleic acid molecule encoding matrix metalloproteinase 1 (SEQ ID NO: 3). As stated in the prior Office Action, Khaw et al. describe matrix metalloproteinase (MMP) inhibitors, especially collagenase inhibitors, and their use in the manufacture of a medicament for the treatment of a natural or artificial tissue comprising extracellular matrix components to inhibit contraction of the tissue and methods for the treatment of tissue comprising extracellular matrix components to inhibit contraction (see col. 1, lines 13-

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16). The MMP inhibitors are designed to inhibit MMPs including MMP-1 (also called collagenase), see col. 1, lines 41-50.

In regards to the targeting of these oligonucleotides to a coding region of a nucleic acid molecule encoding matrix metalloproteinase 1, it was well known to those of ordinary skill in the art at the time the instant invention was made that preferred target regions of mRNA for designing antisense oligonucleotides that are specifically hybridizable with a target mRNA include a transcription initiation site region, a translation initiation codon region, a 5' cap region, an intron/exon junction, coding sequences, a translation termination codon region or sequences in the 5'- or 3'-untranslated region (see Monia et al. col. 5, lines 28-32).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Khaw et al. with the teachings of Brinckerhoff et al. and Monia et al. to design the compounds and compositions according to the present invention. One of ordinary skill in the art would have been motivated to design antisense compounds targeted to the nucleotide sequence of SEQ ID NO: 3, which encodes MMP-1, because Khaw et al. expressly states motivation to design antisense oligonucleotides targeting MMP-1 (col. 9, lines 28-38), and Brinckerhoff et al. provides the nucleotide sequence. Moreover, one of ordinary skill in the art would have been motivated to modify the antisense oligonucleotides of Khaw et al. to comprise phosphorothioate modified internucleoside linkages, 2'-O-methoxyethyl sugar modifications, 5-methylcytosine modified nucleobases, or wherein said antisense compound is a chimeric compound, because according to Monia et al. antisense oligonucleotides comprising these modifications would enhance the cellular properties of antisense oligonucleotides as compared to unmodified antisense compounds. Moreover, one of ordinary skill in the art would have been

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motivated to design compositions comprising the antisense compounds according to the present invention and a pharmaceutically acceptable carrier or diluent, and further comprising a colloidal dispersion system because Monia et al. teach that compositions designed according to this manner would enhance the stability of oligonucleotides introduced into cells and would help to target oligonucleotides to a particular tissue or cell. Additionally, one of ordinary skill in the art at the time the invention was made would have been motivated to design antisense oligonucleotides targeting the coding region of MMP-1 (SEQ ID NO: 3), since Monia et al. clearly teach that the coding region of an mRNA is a preferred target region to design antisense oligonucleotides that are specifically hybridizable to a target mRNA molecule.

Therefore, the invention as a whole remains *prima facie* obvious over Khaw et al. in view of Brinckerhoff et al. and Monia et al.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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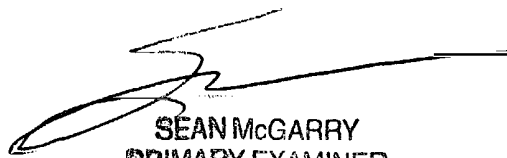
5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 1-571-272-0757. The examiner can normally be reached on Monday-Thursday, 8:30 AM - 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 1-571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps-Ford, Ph.D.
Examiner
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JLE


SEAN MCGARRY
PRIMARY EXAMINER
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